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SUITER WEST PC LLO
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SUITE 220
OMAHA, NE 68154

EXAMINER

HINES, JANA A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 08/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/021,925

Applicant(s)

KIM ET AL.

Examiner

Ja-Na Hines

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 10-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group 1 in Paper No. 7 is acknowledged. Claims 1-37 have been withdrawn from consideration. Claims 1-9 are under consideration in this office action.

This application contains 10-37 are drawn to an invention nonelected without traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

2. The drawings are objected to because of the reasons set forth in the attached PTOL-948. However, the corrections will not be held in abeyance and applicant must submit proposed drawing corrections in response to the requirement in the Office action.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on pages 33-34. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP§608.01.
4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Sequence Compliance

5. This application contains sequence disclosures on at least pages 10 and 16 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for substantially reducing the pathogenicity of an infectious agent, including bacterium, virus or *H.influenzae* without killing said infectious agent, by removing or degrading a surface protein, including an autotransported colonization factor, IgA1 protease, an adhesin and Hap, of said infectious agent, said method comprising contacting said infectious agent with

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substantially pure, non-pasteurized, naturally occurring or recombinant lactoferrin under conditions sufficient to remove or degrade said protein.

The written description in this case only sets forth a specific infectious agent, *H. influenzae*. There is no teaching that viruses have surface proteins which are affected by lactoferrin, i.e., there is no scientific support. Applicants do not even include any characteristics a surface protein of a virus needs which would allow removal or degradation by lactoferrin. Applicants simply state that viruses may be affected. Moreover, not even all bacteria will be affected by the lactoferrin; therefore the method as claimed has not been fully disclosed. The written description is not commensurate in scope with the claims drawn to the method of reducing pathogenicity. Neither the specification nor the claims teach how to reduce the pathogenicity of all infectious agents by contacting any undisclosed surface proteins with lactoferrin. There is no guidance as to what infectious agents actually have susceptible surface proteins; or even what of species of gram-negative bacteria have surface proteins that will be removed or degraded by lactoferrin as claimed. Thus, the claimed method is not taught and/or enabled by the specification. Moreover, there is no teaching that correlates the inactivation of colonization factors to a reduction in pathogenicity.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically infectious agent and surface proteins, the skilled artisan cannot envision the claimed method, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it.

Furthermore, *In The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus.

Therefore the full breadths of the claims fail to meet the written description provision of 35 USC 112, first paragraph.

7. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In particular, claim 1 is drawn to a method for substantially reducing the pathogenicity of an infectious agent without killing said agent, by removing or degrading a surface protein of said agent, said method comprising contacting said agent with substantially pure, non-pasteurized, naturally occurring lactoferrin or recombinant lactoferrin under conditions sufficient to remove or degrade said protein.

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However absent factual evidence, the claims are not enabled for the ability of lactoferrin once it is contacted with any undisclosed surface protein of any infectious agent to remove or degrade the undisclosed protein while not killing the agent and reducing pathogenicity.

The instant specification discloses certain outer membrane proteins of *H. influenzae* are resistant to the removal or degradatory effects of lactoferrin. For example, surface proteins P2, P5 and P6 lack N-terminal passenger domains and are unaffected by lactoferrin. See page 10. Therefore the effects of contacting lactoferrin with any surface protein are largely unpredictable. Moreover, it is well known that lactoferrin resistant microorganisms exists, namely some strains of *Streptococcus pyrogenes*, *Streptococcus lactin*, *Staphylococcus epidermidis*, *E.coli*, *Enterobacter cloacae*, *Salmonella newport* and *Shigella sonnei*. See Arnold et al., (1980). Therefore, the claimed method is unpredictable, as there are known infectious agents and known surface proteins which will not achieve the claimed results. Therefore the claims are drawn to an unreliable correspondence between the claimed yet undisclosed surface protein and the lactoferrin, therefore the claims lack support regarding enablement.

Publications document the unpredictability of the relationship between lactoferrin and surface proteins. Moreover, the claims are not enabled for using surface proteins of viruses and many bacteria species when there is no support for such. It is noted that removing or degrading a surface protein, does not necessarily correlate to a reduction in pathogenicity, but rather if the surface protein was degraded then at best the lactoferrin could inactivate the colonization factors.

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In absence of further guidance from Applicants, the skilled artisan would have to de novo discover what the appropriate infectious agents and surface proteins are and whether an inactivation of colonization factors causing a reduction in pathogenicity. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. The need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for of the method for reducing pathogenicity. Therefore, a skilled artisan would be forced into undue experimentation to practice (i.e., make and use) the invention as is broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-2 and 4-9 rejected under 35 U.S.C. 102(b) as being anticipated by Plaut et al., (WO 97/058840).

The claims are drawn to a method for substantially reducing the pathogenicity of an infectious agent, without killing said infectious agent, by removing or degrading a surface protein, of said infectious agent, said method comprising contacting said infectious agent with substantially pure, non-pasteurized, naturally occurring or recombinant lactoferrin under conditions sufficient to remove or degrade said protein. Dependant claims are drawn to classifying the infectious agent as a bacterium or

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H.influenzae and classifying the surface protein as an autotransported colonization factor, IgA1 protease, an adhesin and Hap.

Plaut et al., teach using lactoferrin to extract IgA protease from gram-positive bacteria. Lactoferrin is available from many mammals and from recombinant sources (page 5 lines 25-32). Lactoferrin has the ability to extract IgA protease from *Streptococcus sanguis*. (page 17 lines 30-35). The membrane bound surface proteins are believed to play a role in the initiation of attachment and colonization of pathogenic bacteria on the surface of saliva-coated teeth (page 187 lines 1-8). By adding lactoferrin to a culture of *S. sanguis*, about 70% of the IgA protease will be released (page 18 lines 10-13). The claims are drawn to a step wherein the surface protein is removed or degraded from the infectious agent wherein lactoferrin is contacted with the agent, here Plaut et al., teach the claimed step for the degradation or removal of the surface protein, IgA protease, by contacting the agent, *S. sanguis* with lactoferrin as claimed. The data indicated that the lactoferrin effect is not limited to gram-negative bacteria (page 18 lines 15-16). Other affected surface proteins include the Hap protein from *H. influenzae* (page 19 lines 7-9). The Hap outer membrane protein is similar to IgA in that they share sequence identity within their catalytic domains (page 19 lines 10-14). Moreover, Hap is a well-known adhesin.

It is noted that the instant specification defines autotransported colonization factors as being IgA proteases and adhesions such as Hap.

With respect to the preamble, the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the

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claimed invention's limitations, therefore the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). If a prior art structure is capable of performing the intended use as recited in the preamble, then it meets the claim. See, e.g., *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). See also MPEP § 2112 - § 2112.02.

Therefore, Plaut et al., anticipate the claims by teaching methods for contacting the infectious bacterial agent with lactoferrin under conditions to remove or degrade the surface protein.

Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Arnold et al., teach bactericidal activity of human lactoferrin. Henderson et al., teach the structure and function of autotransported proteins. Qiu et al., (1995) teach lactoferrin extracts the IgA protease precursor from the outer membrane of *H. influenzae* cells.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers

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for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines *JN*
August 12, 2003

LP
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